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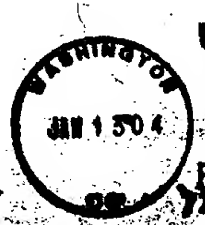

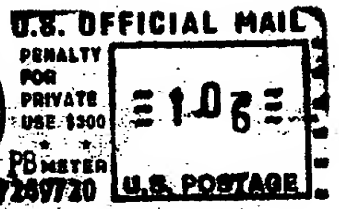

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BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Paper No. 34

Application Number: 07/579,269
Filing Date: September 05, 1990
Appelants: PANICALI ET AL.

Ronald I. Eisenstein
For Appellant

SUPPLEMENTAL EXAMINER'S ANSWER

This is in response to the Remand to the Examiner by the Board mailed August 7, 1998. In the remand, the Board expressed an intention to affirm the Office's rejections under one or more grounds as argued in the Examiner's Answer. However, the Board requested that the Office further consider the 35 U.S.C. § 112, first paragraph rejection in light of a prior art reference cited in the Final Rejection: the Lathe et al. reference. The Board has also requested that the Examiner reconsider the grounds of rejection in light of several previously unconsidered prior art references cited by the Board: the four Paoletti

et al. patents (Paoletti '112, '848, '330, '587), five references cited by Lathe, and the Schlom et al. abstract (Schlom). Upon consideration, the Office concludes, for the reasons set forth below, that the new references do not affect the analysis or rejections of the claims.

The Examiner has considered the four Paoletti patents and has determined that they are less relevant than, and do not add anything to the analysis of the claims over Lathe. The Examiner has also considered the five references cited by Lathe (Lathe references), and has found that they also add little to the determination of patentability of the application and claims at issue. The Lathe references provide little more than background in the art of the invention.

The Schlom reference is not quite so easily dismissed. At first glance, it appears relevant to the rejection based on §101 and §112 paragraph 1 of the United States Code. This reference will be addressed in more detail in the body of this Supplemental Answer, but upon consideration, the Office finds that the Schlom reference does not repair the deficiencies in the application's disclosure such that the claims may be allowed.

However, in light of the Applicants' failure to establish the utility and provide an enabling disclosure of the claimed invention, the Examiner feels that there is no current need to address the 35 U.S.C. § 103 rejections. Therefore, the §103 rejection to claims 15-22 as obvious over Lathe in view of Padhy et al., and further in view of Yamamoto et al. are hereby withdrawn.

1. Status of the Claims

The statement of the status of the claims contained in the Brief is correct. This appeal involves claims 15, 16, 18-22, 36, and 37.

2. Summary of the Invention

The summary of the invention contained in the Brief is correct.

3. Issues

The statement of the issues in the Brief is correct. This Supplemental Answer is intended as an addendum to the previous Examiner's Answer.

4. Grouping of the Claims

The Appellant's Brief states that the claims do not stand of fall together, but fails to provide any support for that statement as required under 37 C.F.R. 1.192(c)(7). The Appellant's statement that all claims are separately patentable is also unsupported.

5. Prior Art of Record

The following are lists of all priori art of record relied on by the Examiner in the Answer, as well as of those references considered by the Examiner for the purpose of responding to the Board's remand.

Prior Art Relied on by Examiner in the Answer

Allen et al., "Specificity of the T-cell Receptor: Two different Determinants are Generated by the Same Peptide and the I-A^k Molecule[1,2]," The Journal of Immunology, vol. 135, pp. 368-73 (1985).

Lathe et al. (Lathe), "Tumor Prevention and Rejection with Recombinant Vaccinia," Nature, vol. 326, pp. 878-80 (1987).

Padhy et al., " Identification of a Phosphoprotein Specifically Induced by the Transforming DNA of RAT Neuroblastomas," Cell, vol. 28, pp. 865-71 (1982).

Yamamoto et al., "Similarity of Protein Encoded by the Human c-erb-B-2 Gene to Epidermal Growth Factor Receptor," Nature, vol. 319, pp. 230-34 (1984).

Additional Prior Art Considered as per the Board's Request

Paoletti et al. (Paoletti '112), 4,603,112, July 29, 1986.

Paoletti et al. (Paoletti '848), 4,722,848, Feb. 2, 1988.

Paoletti et al. (Paoletti '330), 4,769,330, Sept. 6, 1988.

Paoletti et al. (Paoletti '587), 5,110,587, May 5, 1992.

The Lathe References

Drebin et al., "Monoclonal Antibodies Identify a Cell-Surface Antigen Associated with an Activated cellular Oncogene," Nature, vol. 312, pp. 545-48 (1984).

Koprowski et al., "Specific Antigen in Serum of Patients with colon Carcinoma," Science, vol. 212, pp. 53-56 (1981).

Peto, R. & H. Zur Hausen (Eds.), Banbury Report 21, Viral Etiology of Cervical Cancer, Cold Spring Harbor Laboratory, New York (1986).

Real, F.X. et al., "Class 1 (Unique) Tumor Antigens of Human Melanoma," Journal of Experimental Medicine, vol. 160, pp. 1219-33 (1984).

Ueda, R. et al., "Cell Surface Antigens of Human Renal Cancer Defined by Autologous Typing," Journal of Experimental Medicine, vol. 150, pp. 564-72 (1979).

6. Grounds of Rejection

This Supplemental Answer continues the analysis of the rejections based on 35 U.S.C. §101 and §112 paragraph 1.

7. Supplementary Response to the Argument

The claimed invention is a method of immunizing humans against human cellular oncogene encoded products by inoculating them with either a pox or vaccinia virus expressing the oncogene, proto-oncogene, or homologue thereto (all 3 inclusively

referred to as "oncogene"). The Appellants' claims have been rejected under 35 U.S.C. §101 for failure to establish the invention's utility, and under §112 paragraph 1 for failure to provide an enabling disclosure of the invention. Section 101 reads as follows:

> "Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title."

All of the claims at issue in this appeal are rejected under this section for failure to establish utility. As was argued in the Answer, this failure arises because the appellant's disclosure does not show that inoculating an individual with a virus expressing an oncogene (by expressing the oncogene product) would immunize that individual from tumors expressing such products.

In the Answer, the Examiner argued that the specification failed to show that such an inoculation would immunize an individual against tumors expressing oncogene products. The specification showed that while such an inoculation into mice seemed to cause them to reject tumors expressing the oncogene products, use of the same inoculation into rates failed to promote tumor rejection in rats. This showed that the mice could have been reacting because the oncogene was a foreign substance rather than because an immune response had been elicited. The failure of the rats to reject rat tumors expressing rat oncogene products created doubt that the claimed method would work in any situation where the subject was inoculated with a virus expressing a syngenic oncogene. This, in turn, created a question as to whether the claimed method would cause a human to reject tumors expressing human oncogene products. Thus, utility has not been shown.

Likewise, because the disclosure demonstrated that syngenic test subjects did not respond to the inoculation as the applicant claimed they should, the claims have not been enabled. Section 112 paragraph 1 of 35 U.S.C. reads as follows:

> "The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise and exact terns as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor for carrying out the invention."

The invention has not been enabled because the appellant did not show that the disclosed method of immunization would in fact immunize a human against a human oncogene product. Because the claimed method did not elicit an immune response in rate against rat oncogenes, the appellant has not shown that a human could be immunized against human oncogenes using the disclosed method. Since the method has not been shown to work, it is not enabled as required by §112 paragraph 1.

Effect of the Schlom Reference

The Schlom reference is an abstract of an article explaining the results of clinical trials of the disclosed method. The abstract states that the inoculation of a vaccinia virus expressing the human carcinoembryonic antigen (CEA) into cancer patients did yield an improved immune (CTL) response in those patients against cancer expressing CEA. However, while this may be encouraging, it is not sufficient to overcome the current rejections to the claims.

The claims on appeals all cover a virus expressing an oncogene, proto-oncogene, or an oncogene or proto-oncogene homologue product. See the Appendix to the Appeal Brief. Such genes have the potential to cause transformation of normal cells into tumor

cells if mutated from their wild-type form. Application, pp. 1, 3-4. Oncogenes may encode for proteins that operate inside the cell, or for cell surface proteins with internal effects (e.g. growth factor molecules). Application, pp. 3-4. The Applicant used an oncogene product in the viral antigen disclosed in the application pp. 24-36. It was this disclosed, oncogene product antigen that failed to work, thus giving rise to the rejections both for lack of utility and enablement.

Along with the oncogenes, Appellant's disclosure also mentioned another type of gene product that may be used in the immunization method disclosed. Application, p. 8. These tumor-associated molecules are not expressions of oncogenes, or even necessarily involved in cell transformation. Nevertheless, these molecules are still associated with tumors because they are expressed by tumor cells. Application, p. 8. The Appellants list CEA, the molecule tested in the clinical trials, as such a tumor-associated molecule, not as an oncogene product, pp.8.

Tumor-associated molecules are not expressions of oncogenes, and therefore do not fall within the invention claimed by the appellant. Genes encoding these molecules do not have the potential to transform cells, even where they may be involved in transformation, as do the oncogene antigens. The tumor-associated molecules are distinct from those molecules consisting if oncogene products. Similarly, the inoculation in the Schlom reference is distinct from the claimed invention. The effectivity of viral antigens using tumor-associated molecules does not establish to the patentability of the claimed method, which uses oncogene products as the antigen.

Nor can the successful use of such distinct molecules in a disclosed, but unclaimed, mode of use overcome a rejection based on an unsuccessful test of the

claimed method. Here, the claims are rejected because the Application failed to show the utility of, and to enable, the claimed mode of practicing the invention; i.e. using a viral antigen expressing an oncogene product. The Schlom reference does not relate to the claimed method. It shows only that a related, and disclosed, method may work. It is not sufficient to overcome the earlier evidence in the Application suggesting the inoperability of the claimed method itself. Thus, the Schlom reference does not establish utility of the invention, nor does it enable the disclosure. The reference is therefore not relevant in the present case.

Further Consideration of Lathe

Lathe discloses the use of recombinant vaccinia to elicit tumor immunity responses for tumors caused by the tumorigenic properties of the Polyoma virus. The authors of that reference took three tumor-specific antigens, three different early Polyoma proteins, and inserted each of the three into a different vaccinia recombinant. They found that two of the three recombinant vaccines lead to a regression of and, under certain circumstances, to an elimination of Polyoma transformed tumor cells injected into test animals. Their experiments showed that they could get such results in rats vaccinated both before and after inoculation with the tumor cells. While this reference does show potential promise for the future use of recombinant viral antigens in eliciting immune responses to tumors, it does not fill in the gaps of the Appellants' disclosure such that either the utility or enablement requirements are satisfied.

Lathe does not deal with syngenic oncogenes, as does the Appellants' invention, but with tumor-associated viral proteins. One of the elements of the Appellants' claimed invention is that the immune response be against a syngenic oncogene's product. The

Appellants' claims were rejected because they did not get such an immune response in response to inoculation with a viral antigen expressing that oncogene. Recognition of a foreign protein in an immune response is not a satisfactory substitute for recognition of a syngenic protein. Thus, Lathe is not relevant to the consideration of the claims under 35 U.S.C. § 101 and § 112 paragraph 1.

For the reasons stated above, it is believed that the rejections should be sustained.

This Application has been forwarded to the Board of patent Appeals and interferences for decision on the Appeal.

Respectfully submitted

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